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Selenium, Glutathione Peroxidase and Oxidative Hemolysis in Sickle Cell Disease

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Oxidative damage of red cell membrane is known to be accelerated in sickle cell disease. However, the exact mechanism of this acceleration is unclear. We have read with interest the recent article entitled 'Selenium and Glutathione Peroxidase Levels in Sickle Cell Anemia' by Natta et al. [1]. They reported that a modest decrement of glutathione peroxidase activity could have been partly responsible for accelerated peroxidation of the red cell membrane resulting in hemolytic anemia.

Since the enzyme contains selenium as selenocysteine at its active site, selenium deficiency results in decreased enzyme activity. However, New Zealand residents are hematologically normal in spite of decreased enzyme activity due to low intake of selenium. Although glutathione peroxidase deficiency was found in healthy newborn infants whose selenium content in plasma was low and has been considered to be responsible for neonatal hyperbilirubinemia, prospective studies on 194 infants have failed to demonstrate a clear correlation between glutathione peroxidase levels and serum bilirubin levels. In addition to variations in the selenium content, a deficiency of this enzyme also occurs as a genetic polymorphism in asymptomatic Mediterranean and Jewish populations. To date, therefore, it is widely accepted that there is no convincing evidence for a cause-and-effect relationship between enzyme activity and hemolytic anemia [2-4].

Sickle cell erythrocytes show increased susceptibility to lipid peroxidation. It was previously reported that glutathione peroxidase protected the membrane against lipid peroxidation in the presence of reduced glutathione by reducing lipid hydroperoxides to lipid alcohols. Contrary to earlier studies, from our laboratory [5, 6] and other laboratories [7-11], recently accumulated evidence indicates that glutathione peroxidase is not responsible for the protection against lipid peroxidation in red cells or other tissues [12]. In fact, it was experimentally confirmed by Grossman and Wendel [13], who showed that phospholipid hydroperoxides are not reduced by glutathione peroxidase. Although Ursini et al. [14] reported about selenium-containing glutathione peroxidase which acted upon phospholipid hydroperoxide in membrane structure, it was different from 'classical' selenium glutathione peroxidase.

There is another argument that removal of hydrogen peroxide by glutathione peroxidase in vivo will decrease the formation of hydroxyl radicals by the Fenton reaction and will thus prevent one route for the initiation of peroxidation [15]. Until recent years, it was believed that glutathione peroxidase is the major route for disposing of hydrogen peroxide under physiologic conditions

and catalase does not play an important role in protecting erythrocytes against endogenous hydrogen peroxide. However, the latest study demonstrated that these two routes are equally involved in the removal of hydrogen peroxide in human erythrocytes [16]. Failure of only one of the mechanisms may not be deleterious.

Moreover, there have been a couple of papers describing increased glutathione peroxidase activity in sickle erythrocytes [17,18].

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